Complete Summary

GUIDELINE TITLE

Management of chronic kidney disease and pre-ESRD in the primary care setting.

BIBLIOGRAPHIC SOURCE(S)

Veterans Health Administration, Department of Defense. VHA/DoD clinical practice guideline for the management of chronic kidney disease and pre-ESRD in the primary care setting. Washington (DC): Department of Veterans Affairs (U.S.), Veterans Health Administration; 2001 May. Various p.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Chronic kidney disease and pre-end stage renal disease (ESRD)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Nephrology
Urology

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To identify patients at risk for progression of renal disease or patients with reversible conditions
- To promote the recognition of abnormal renal function
- To slow the progression of renal disease
- To prevent or treat metabolic, hematologic, and cardiovascular abnormalities
- To describe the referral points to specialty care
- To encourage the preparation of the patient for end stage renal disease (access) at an appropriate time

TARGET POPULATION

Any person with persistent elevated creatinine or proteinuria who is eligible for care in the Veterans Health Administration (VHA) or Department of Defense (DoD) health care delivery system

INTERVENTIONS AND PRACTICES CONSIDERED

Assessment/Diagnosis

1. Patient history, physical examination, and laboratory tests
2. Assessment of renal function (estimation of creatinine clearance using serum creatinine and quantitation of proteinuria)
3. Performance of diagnostic work-up, including urinalysis (urine dipstick), proteinuria, complete blood count, serum electrolytes, blood urea nitrogen (BUN), serum creatinine, glucose, albumin, total protein, glomerular filtration rate (GFR), cholesterol, renal ultrasound)
4. Consultation or conferral with nephrologist, as necessary
5. Discussion with patient of future need for renal replacement therapy

Management/Treatment

1. Treatment of underlying disorder leading to renal disease (hypertension, diabetes mellitus, glomerulonephritis, polycystic renal disease, urinary tract obstruction, analgesic nephropathy, HIV-associated nephropathy, renovascular disease)
2. Initiation of strategies to slow the progression of renal disease, including control of hypertension, use of angiotensin-converting-enzyme inhibitors (ACE-I), protein restriction, and control of hyperglycemia in diabetics
3. Prevention and treatment of symptoms and complications:
    - Management of metabolic abnormalities (maintenance of potassium, calcium, phosphate balance; prevention of hypoalbuminemia and metabolic acidosis)

- Management of hematologic abnormalities (evaluation of anemia and determination of serum ferritin, oral iron therapy, epoietin therapy)
- Management of volume overload (weighing at every visit, sodium restriction, loop diuretics, initiation of dialysis)
- Maintenance of adequate nutrition, including protein restriction

4. Prevention and treatment of cardiovascular disease
5. Patient education about renal disease and self-management
6. Follow-up

MAJOR OUTCOMES CONSIDERED

- Accuracy of diagnostic tests
- Rate of progression of renal disease
- Complications of renal disease
- Patient acceptance and compliance

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The algorithm and annotations were based on an exhaustive review of the literature. The goal of the literature review was to provide a systematic basis for the development of an evidence-based guideline. The inclusion criteria for the literature search were related to the population being studied (adult) and the treatment setting (primary care).

The Medical Subject Headings (MeSH) terms used for the search included key therapies in chronic renal disease and end stage renal disease (ESRD), study characteristics, and study design. In this search, "study characteristics" were those of analytic studies, case-control studies, retrospective studies, cohort studies, longitudinal studies, follow-up studies, prospective studies, cross-sectional studies, clinical protocols, controlled clinical trials, randomized controlled trials (RCTs), intervention studies, and sampling studies. Study design included crossover studies, double-blind studies, matched pair analysis, meta-analysis, random allocation, reproducibility of results, and sample size.

NUMBER OF SOURCE DOCUMENTS

40 source documents

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The rating scheme used for this guideline is based on a system used by the U.S. Preventive Services Task Force (USPSTF, 1996). This scheme is as follows:

Quality of Evidence:

I. Evidence obtained from at least one properly randomized controlled trial.

II-1. Evidence obtained from well-designed controlled trials without randomization.

II-2. Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one center or research group.

II-3. Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III. Opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

The "Quality of Evidence" rating is based on the quality, consistency, reproducibility, and relevance of the studies. Information about harmful effects must also be presented.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Forty articles were identified for inclusion in a table of information that was provided to each expert participant. The table of information contained: Title, Author(s), Author(s) affiliation, Publication type, Abstract, Source, Relevance. Copies of these tables were made available to all participants. Copies of specific articles were provided on an as needed basis.

The working group reviewed articles for relevance and graded the evidence using the rating scheme, published by the U.S. Preventive Services Task Force (USPSTF, 1996).

The experts themselves, after an orientation and tutorial on the evidence grading process, formulated quality of the evidence (QE) and strength of the recommendations (SR) ratings. Each reference was appraised for scientific merit, clinical relevance, and applicability to the populations served by the Federal health care system. Recommendations were based on consensus of expert opinions and clinical experience only when scientific evidence was unavailable.

The assembled experts were an invaluable source of additional information and suggested numerous references. These were distributed to participants on an as

needed basis. It must be noted that the guideline document does not, however, include reference to any publications dated after December, 1999.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Once the evidence tables were developed, a group of not more than 20-30 champions and other key clinical leaders were identified and convened to evaluate the evidence and develop the guideline in accordance with it.

To make actual recommendations, the clinical experts, led by the designated National Guideline Champions, interpreted the evidence, assessed its generalizability and its applicability to the population of interest, and assessed the overall strength of evidence for the recommendation. Recommendations based solely on clinical judgement and experience were scrutinized to eliminate bias and self-interest. This group of clinical experts also developed consensus-based recommendations.

Follow up conference calls were conducted to discuss unresolved issues and compile the annotations of the guideline. The resulting product was the draft of the guideline to be distributed for comment.

The draft of the guideline was posted on a development website for field review and comment: Patient Care Services and the Network-appointed Guideline Champions solicited feedback from a broader group of end users. Network designated staff were asked to use the guideline in the direct care setting and provide feedback to the Network Guideline Champions and/or directly to the guideline development experts via the web page which is available for online comment. This portion of the field tests is more specifically directed towards an evaluation of the content and the logic and flow of the guideline. Comments and recommendations regarding proposed changes to the content of the guideline must have been supported by evidence. The National Guideline Champions replied to the respondents and integrated comments and suggestion into the evidence review as appropriate.

Champions and other key clinical leaders re-convened to finalize the guideline: A group of champions and other key clinical experts, or a sub group selected by the National Senior Champions, were reconvened to integrate the comments of the reviewers, as appropriate, to complete the guideline.

Following the face-to-face meeting, the group re-convened by conference call to review and finalize the guideline to be distributed for field testing.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The rating scheme used for this guideline is based on a system used by the U.S. Preventive Services Task Force (USPSTF, 1996). This scheme is as follows:

Strength of Recommendation:

A. There is good evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
B. There is fair evidence to support the recommendation that the condition be specifically considered in a periodic health examination.
C. There is insufficient evidence to recommend for or against the inclusion of the condition in a periodic health exam, but recommendations may be made on other grounds.
D. There is fair evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.
E. There is good evidence to support the recommendation that the condition be excluded from consideration in a periodic health examination.

The "Strength of Recommendation" rating is influenced primarily by the science, although other factors are also taken into consideration.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations for the management of chronic renal disease and pre-end stage renal disease (ESRD) in the primary care setting are formatted as a single algorithm. The algorithm, the objectives, and annotations that accompany it are presented below.

Algorithm - Management of Chronic Kidney Disease and Pre-End Stage Renal Disease (ESRD) in the Primary Care Setting.

A. Patient with Persistent Elevated Creatinine or Proteinuria (above Normal Limits)

   This guideline should be used for patients in need of further diagnostic work-up, treatment and follow-up. These patients present to primary care and are found to have:

- Persistent elevated serum creatinine; serum creatinine (SCr) levels above the upper limit of normal for the laboratory on two consecutive tests

  and/or

- Proteinuria (>1+) on dipstick, confirmed on two tests

This guideline applies to patients presenting with proteinuria or elevated serum creatinine and to patients being followed for chronic renal disease. The presence of proteinuria may indicate renal disease even with a normal serum creatinine. Renal insufficiency is the asymptomatic stage of reduced renal function with serum creatinine elevated above normal. Any of these patients has a potentially serious renal disease that might progress to renal failure.

Note: Pure hematuria is usually a urologic problem. If a referral is needed after the initial workup by primary care, it should be to urology and not nephrology.

Assessment - Diagnosis

B. Obtain History, Physical Examination and Laboratory Tests

The objective is to identify the clinical markers that indicate renal disease and to outline basic diagnostic testing required in all patients.

History, physical exam, and basic laboratory evaluation remain the cornerstone for diagnosis in patients presenting with renal disease.

History:

- Chronic medical problems:
  - Diabetes
  - Hypertension
  - Prior renal disease
  - Collagen vascular disease
  - Hepatitis
  - HIV
  - Renal stones
  - Prostate disease
- Attention to symptoms associated with renal disease such as:
  - Decreased attentiveness
  - Nausea/vomiting, anorexia, weight change
  - Dyspnea, orthopnea, leg swelling
  - Fatigue, muscle cramps, restless legs, peripheral neuropathy
  - Pruritus
  - Urinary urgency, frequency, nocturia, dysuria
- Medications/over-the-counter products (nonsteroidal anti-inflammatory drugs [NSAIDs], angiotensin-converting-enzyme inhibitors [ACEIs], angiotensin receptor blockers, diuretics, analgesics, antibiotics, antiviral agents, lithium)

- Family history of renal disease (polycystic renal disease [PCKD])

Physical Examination:

- Height, weight
- Vital signs including orthostatic blood pressure
- Volume assessment (rales, jugular venous distention, peripheral edema, cardiac heave/gallop/rub)
- Vascular exam (pulses, bruits)
- Abdominal findings (mass, bruit, palpable bladder, flank tenderness)
- Digital rectal exam (prostate) in men
- Neurological exam
- Integument (rash, stigmata of embolic disease or ischemia)
- Joints (arthritis)

Basic Laboratory Evaluation:

- Sodium (Na), potassium (K), chloride (Cl), carbon dioxide (CO_2), blood urea nitrogen (BUN), serum creatinine (SCr), glucose, calcium (Ca), phosphate (PO_4), albumin, total protein, cholesterol
- Urinalysis and review of urinary sediment
- Complete blood count (CBC) with differential

C. Emergent, Urgent Condition?

The objective is to identify patients with acute (potentially reversible) renal disease or life-threatening conditions who require immediate attention.

Rapidly increasing serum creatinine (25% increase over days) requires urgent investigation.

The initial evaluation should determine whether a patient has manifestations of renal disease that require emergent or urgent intervention such as:

- Fluid overload, especially pulmonary edema
- Hyperkalemia
- Metabolic acidosis
- Pericarditis
- Encephalopathy
- Uremic symptoms such as nausea, vomiting and anorexia

Acute renal dysfunction is frequently reversible. Patients with any acute component require prompt medical intervention.

The most common causes of acute renal dysfunction include:

- Volume depletion
- Severe heart failure
- Urinary tract obstruction
- Acute tubular necrosis (ATN)
- Acute interstitial nephritis
- Acute pyelonephritis

- Acute glomerulonephritis
- Atheroembolic disease

D. Assess Renal Function

Objective

To determine the current level of renal function.

Annotation

Assessment of renal function involves estimation of the creatinine clearance (Clcr) using serum creatinine (SCr) and quantitation of proteinuria.

Creatinine clearance can be estimated by using the Cockcroft-Gault formula:

For males: (140 - age)/SCr (mg/dL)x wt (kg) /72
For females x by 0.85

The 24-hour urine collection for creatinine clearance approximates the glomerular filtration rate (GFR). It is less accurate than the formula, however,

For quantitation of proteinuria use a spot urine protein/creatinine ratio.

E. Perform Diagnostic Work-up

Objective

To establish the etiology of renal disease.

Annotation

Perform specific lab tests or special studies to define the cause of:

- Persistently elevated creatinine
- Persistent proteinuria

The complete history and physical must precede and guide the diagnostic work-up. Additional tests and imaging studies should be considered if indicated.

Diagnostic tests:

- Urinalysis
- Quantitate proteinuria
- CBC
- Na, K, Cl, CO_2, BUN, serum creatinine, glucose, Ca, PO_4, albumin, total protein
- Estimated glomerular filtration rate
- Cholesterol
- Renal ultrasound should be ordered:

- To evaluate for urinary tract obstruction
- To estimate the size of the renal
- To evaluate for polycystic renal disease

The urinalysis reagent dipstick for protein and blood gives the important initial information regarding the type of disease that may be causing renal disease or proteinuria. (see "Urine Dipstick: Interpretation", below)

Urine Dipstick: Interpretation

Protein negative, blood negative: Consider false negative, rule out microalbuminuria, rule out multiple myeloma and other paraproteinuria, consider pre-renal cause, consider post-renal cause, consider ischemic nephropathy,

Protein positive, blood negative: Rule out false positive, benign or orthostatic proteinuria; consider hypertension (HTN), nephrosclerosis, diabetes, tubulo-interstitial diseases, polycystic renal disease (PCKD), glomerular nephritis (GN), etc.; quantitate protein

Protein positive, blood positive : Consider urinary tract infection (UTI), pyelonephritis, rapidly progressive glomerular nephritis (RPGN), glomerular nephritis, HIV vasculitis, pulmonary-renal syndrome, hemolytic uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP), malignant hypertension, nephrotic syndrome, nephrolithiasis with obstruction, atypical diabetes mellitus, cystic renal disease

The degree of proteinuria further defines the cause of the persistent elevated creatinine and/or the cause of the abnormal proteinuria. (See "Evaluation of Proteinuria", below)

An etiologic evaluation should be guided by history and physical, urinary sediment and degree of proteinuria. (See Appendix 1, "Etiologic Evaluation" in original guideline document)

A guide to specialized laboratory studies for the diagnosis of renal disease can be found in Appendix 2 in original guideline document.

Evaluation of Proteinuria

j. Spot protein creatinine ratio estimates 24-hour excretion of protein in grams/24 hr. To perform the test, a random urine sample is submitted to the laboratory for protein concentration (in mg/dL) and creatinine concentration (in mg/dL). The protein concentration is divided by the creatinine concentration, and the unit-less number is the estimated daily protein excretion in gm/24 hrs. An abnormal ratio is >0.15, which estimates a 24 hour protein excretion of >150 mg/day (>0.15 gm/day). Many nephrologists recommend using

protein:creatinine ratios to quantify protein excretion instead of a 24 hour urine collection.

k. Further define cause based on degree of proteinuria:

normal: <150 mg/24hr

microalbuminuria: 30-300 mg/24 (specifically albumin; usually measured in diabetics)

trace proteinuria: 150 to 500 mg/24 hr

mild proteinuria: 500 mg to 1 g/24 hr

moderate proteinuria: 1-3 g/24 hr

nephrotic range proteinuria: >3 g/24 hr

l. Types of proteinuria:

1. Overflow proteinuria: Trace or negative dipstick protein but disproportionate larger amount on 24 hr. test. Its presence suggests: light-chain, paraproteinemia, lymphoproliferative process, or hemolysis (only if dip also blood +).
2. Tubular protein: 500 mg – 2000 mg/24 hours. Differentiate from glomerular causes by urine protein electrophoresis +/- immunoelectrophoresis (UPEP+/-IEP)
Urine protein electrophoresis: albumin >globulin suggests glomerular proteinuria; globulin >albumin suggests light chains or paraproteinemia

Some common causes include analgesic nephropathy, focal glomerular sclerosis (recurrent urinary tract infection, reflux), collagen vascular diseases (Sjogren's syndrome, lupus), hepatitis, HIV, polycystic renal disease, heavy metal toxicity, interstitial nephritis (drugs or infectious), granulomatous diseases, etc.

3. Glomerular protein, suggested by moderate to heavy proteinuria.
Suggests a more serious disorder.
Significant glomerular damage with proteinuria of >3 grams: refer to nephrologist.
Rule out diabetes progression, hepatitis, HIV, vasculitis, malignancy, glomerulonephritis, etc.

4. Massive proteinuria (>6 gm/24 hours)
Focus history and physical to rule out HIV, hepatitis-associated nephropathy (HAN), severe

focal glomerulosclerosis, etc. Refer to nephrologist.

F. Is There an Acute Exacerbation of Established Renal Disease?

Objective

To identify acute deterioration of renal function in a patient with established renal disease.

Annotation

Patients with established chronic renal disease might also develop acute renal failure due to a new illness, or as a complication of therapy. Any worsening of renal function, especially if it occurs over a short time period, should be considered acute renal failure, and evaluated promptly. Only after acute renal failure is ruled out can deterioration in renal function be ascribed to progression of the patient's underlying chronic disease.

Common causes of acute deterioration in renal function include:

- Medications (angiotensin-converting-enzyme inhibitors, NSAIDs, angiotensin II receptor blockers [ARBs] and many others)
- Volume depletion
- Urinary tract obstruction or infection
- Radiographic contrast
- Worsening congestive heart failure
- Renal vascular disease (aortic dissection, cholesterol embolization)
- Sepsis
- Rhabdomyolysis or hemolysis

G. Is Serum Creatinine >4 mg/dL or Creatinine Clearance <25 or Symptoms of Chronic Renal Failure?

Objective

To ensure that all patients who might benefit from renal replacement therapy will have the options presented to them in a timely manner to permit adequate preparation for renal replacement therapy.

H. Is Serum Creatinine $\geq$2.0 mg/dL ($\geq$ 1.5 female) or Glomerular Filtration Rate $\leq$50 ml/min or Nephrotic Range Proteinuria or Questionable Etiology of Renal Disease?

Objective

To identify individuals with renal disease who are at risk for progression, who require further diagnostic procedures, or who will benefit from early consultation with the nephrologist.

Annotation

All patients with established renal disease are at risk for progression and may require interventions to slow the progression, prevent complications, and reduce symptoms. The primary care provider should institute these interventions. Severity of the renal function indicated by serum creatinine $\geq$2.0 mg/dL (or glomerular filtration rate $\leq$50 ml/min) is usually associated with progression of the renal disease; therefore a nephrologist can assist the primary care provider in managing the disease and its associated complications.

In patients with nephrotic range proteinuria or renal disease of unknown etiology the nephrologist will make the diagnosis and recommend treatment. Renal biopsy may be recommended to determine the histopathology of the renal disease.

Treatment

I. Consult/Confer with Nephrologist

The objective is to obtain the assistance of a specialist for either diagnostic or management issues.

Referral to a nephrologist may be helpful to the primary care provider to:

- Assist with diagnosis of the cause of renal disease, including renal biopsy
- Assist in ruling out reversible causes of elevated creatinine such as urinary tract obstruction
- Reinforce the need for aggressive blood pressure control and dietary management to slow the progression of the disease
- Jointly manage various complications of renal insufficiency such as:
    - electrolyte disorders
    - secondary hyperparathyroidism
    - anemia secondary to erythropoietin deficiency
    - metabolic acidosis

J. Discuss Future Need for Kidney Replacement Therapy

The objective is to prepare the patient, in a timely and effective manner, for eventual kidney replacement therapy.

Counseling by Primary Care:

- Development of end stage renal disease (ESRD) is emotionally traumatic for most patients
- Patients who learn to accept end stage renal disease have better compliance and better outcomes
- Advantages of early discussion about end stage renal disease and renal replacement therapy options:
    - Assists in emotionally preparing patient for lifestyle changes
    - Trust and continuity established by primary care aids nephrologist

    - Allows time for preparation and consideration of home dialysis and living related donor (LRD) transplant
- Simple steps that can be taken in the primary care setting:
    - General discussion about progression of renal disease to end-stage renal disease
    - Explanation of why patient needs to see nephrologist
    - Reinforce and review information provided to patient by nephrologist
    - Discuss in general terms principles of dialysis (hemodialysis [HD] and peritoneal dialysis [PD]) and transplantation
    - Maintain consistency of information between primary care and nephrologist.

Indications for Initiation of Kidney Replacement Therapy

The indications for the initiation of dialysis are controversial. Some authors advocate early initiation of dialysis, prior to the development of symptoms, based on the assessment of glomerular filtration rate. They contend that early uremia is associated with impaired nutritional intake and progressive malnutrition, and advocate the initiation of kidney replacement therapy with "incremental" dialysis, progressively increasing the dose of dialysis as residual kidney function declines. In contrast, other experts advocate the use of aggressive protein restriction with supplementation of essential amino acids to postpone the development of uremic symptoms, contending that nutritional status can be maintained with this approach.

In light of the above controversy, the following can be used to guide initiation of kidney replacement therapy after attempts have been made to optimize dietary protein and caloric intake.

Indications For Initiation of Kidney Replacement Therapy

Absolute Indications for Dialysis

- Advanced uremia
    - Uremic pericarditis
    - Uremic encephalopathy
    - Uremic pancreatitis
- Metabolic disturbances refractory to medical management
    - Hyperkalemia
    - Metabolic acidosis
- Uremic symptoms not amenable to dietary modification
    - Severe nausea and vomiting
    - Anorexia with weight loss
    - Uremic encephalopathy
    - Neuropathy
- Refractory volume overload
    - Congestive heart failure
    - Pulmonary edema
    - Peripheral edema with skin breakdown

Relative Indications for Dialysis

- Estimated glomerular filtration rate <10 mL/min/1.73m^2 (Kt/V urea <2.0), unless:
    - Lean body mass is stable or increasing

      and

    - Normalized protein nitrogen appearance rate (nPNA) > 0.8 g/kg/day
- Estimated glomerular filtration rate of 10-20 mL/min/1.73m^2 with signs of malnutrition (normalized protein nitrogen appearance rate < 0.8 g/kg/day or loss of lean body mass)
- Moderately severe to severe volume overload

K. Manage Primary Etiology of Renal Disease: Diabetes Mellitus, Hypertension, Glomerulonephritis, Urinary Tract Obstruction, Analgesic Nephropathy, Polycystic Kidney Disease, HIV-Associated Nephropathy, Hepatitis C Virus, Renovascular Disease, Multiple Myeloma or Other

The objective is to treat the primary cause(s) of renal disease.

Treatment of the underlying disorder leading to renal disease may delay, prevent or reverse the progression of renal insufficiency. In the majority of cases the etiology of the renal disease has previously been determined (see Box 5 or 11 in the original guideline document).

1. Hypertension: See the National Guideline Clearinghouse (NGC) summary of the Veterans Administration/Department of Defense (VA/DoD) guideline: Diagnosis and Management of Hypertension in the Primary Care Setting.
2. Diabetes Mellitus: See the Veterans Administration/Department of Defense guideline: The Management of Diabetes Mellitus in the Primary Care Setting.
3. Glomerulonephritis

   Glomerulonephritis includes multiple diseases, each of which may require different treatments. The nephrologist will determine the specific treatment of Glomerulonephritis.

4. Polycystic Kidney Disease

   Because of the systemic nature of polycystic kidney disease and its detailed implications for patient and family counseling, a diagnosis of polycystic kidney disease should prompt a referral to nephrology, at least for initial evaluation and recommendation. Although there is no specific treatment, periodic follow-up by a nephrologist is recommended. Nephrology consultation should be sought for any polycystic kidney disease patient with urinary tract infection, for appropriate antibiotic selection.

5. Urinary Tract Obstruction

The treatment of urinary tract obstruction is relief of the obstruction, which may require referral to a urologist. The patient with urinary tract obstruction may also have infection, which should be treated.

Patients should receive follow-up after diagnosis and relief of urinary obstruction to determine whether renal function has normalized. Serum creatinine may require several weeks to reach a steady state, and may never return to normal. Should renal failure not resolve within weeks, alternative causes for renal dysfunction, or new acute renal failure should be considered. Nephrology should be consulted if serum creatinine remains greater than 2 mg/dL.

6. Analgesic Nephropathy

Analgesic nephropathy is caused by chronic use of NSAIDS (e.g., indomethacin, fenoprofen, naprosyn, ibuprofen etc.) or abuse of combination analgesics (e.g., aspirin, acetaminophen). Cessation of the offending agent(s) may improve renal function.

7. HIV-Associated Nephropathy and Hepatitis C Virus-Related Kidney Disease

Evidence of kidney abnormalities (elevated serum creatinine, proteinuria and/or hematuria) in HIV infected individuals should prompt early evaluation by the nephrologist. The spectrum of kidney disease seen in HIV positive patients includes HIV-associated nephropathy, immune-complex mediated glomerulonephritis and acute kidney failure syndromes. Kidney biopsy may be required to determine the etiology of the renal failure.

Management of HIV-analgesic neuropathy may include the use of anti-retroviral medications and angiotensin converting enzyme inhibitors. Use of corticosteroids is controversial. Testing for both hepatitis B virus (HBV) and hepatitis C virus (HCV) should be performed in HIV positive individuals with renal disease.

Evidence of renal disease in hepatitis C virus-positive individuals requires early nephrologic consultation. Renal disease may exist in the absence of active hepatitis. The most common renal disease found in these patients is membrane proliferative glomerulonephritis, which may be associated with cryoglobulinemia. Testing for complement levels and the presence of cryoglobulins may be initiated prior to referral. Renal biopsy may be required in many cases to confirm the etiology of the renal disease. Treatment of this entity may include alpha interferon and ribavirin and should only be administered after consultation with a renal specialist.

8. Renovascular Disease

The indications for the treatment of renal artery stenosis associated with chronic kidney insufficiency (CKI) are controversial. Although there is some evidence that intervention with surgery or angioplasty

may reverse or stabilize kidney function, the natural history of untreated atherosclerotic renal artery stenosis is not well characterized. In the absence of randomized controlled studies, patients with known renal artery stenosis should be referred to a nephrologist if they have hypertension that is difficult to control, or if they experience an increase in creatinine of > 25% in less than six months.

The patient with bilateral renal artery stenosis is at risk for development of worsening renal function or hyperkalemia with the use of angiotensin converting enzyme inhibitor or angiotensin receptor blockers. Although these drugs may be used safely in most patients with unilateral renal artery stenosis, such patients require careful monitoring. Serum creatinine and potassium should be determined within 2-4 weeks of initiating therapy or increasing dosage. Angiotensin converting enzyme inhibitor have been found to be effective in ameliorating diabetic and non-diabetic renal disease when proteinuria is present. They should be used cautiously in patients with suspected renovascular disease including patients with unilateral, bilateral or small vessel disease i.e. ischemic nephropathy because angiotensin II is very important in maintaining glomerular filtration rate when vascular perfusion is impaired. Usually these patients exhibit progressive renal failure but scant proteinuria.

9. Multiple Myeloma With Monoclonal Immunoglobulin Light Chain-Related Renal Diseases

Elevated serum creatinine may be the initial presentation in patients with multiple myeloma or other paraproteinemias. Disease entities associated with monoclonal gammopathies include multiple myeloma, undefined plasma cell dyscrasia, AL amyloidosis, chronic lymphocytic leukemia. Management of monoclonal light chain-related renal disease requires abolishing the production of immunoglobulin light chains. Special attention should be given to avoidance of all nephrotoxics like nonsteroidal anti-inflammatory drugs, radiocontrast dye, and dehydration.

L. Initiate Strategies to Slow the Progression of the Disease

Objective

To retard the progression of renal disease by the use of non-invasive interventions.

Annotation

The strategies to slow the progression of the disease include:

- Control of hypertension
- Use of angiotensin converting enzyme inhibitor
- Protein restriction

- Control of hyperglycemia in diabetics.

4. Control of hypertension

   In patients with chronic renal disease, progressive glomerulosclerosis results in a progressive loss of renal function, even when the initial renal insult has been removed. Vigorous control of hypertension reduces the glomerular capillary pressure and slows the progression of glomerulosclerosis. The goal blood pressure should be <125/75 or mean arterial pressure less then 92 for patients with proteinuria and 130/85 in patients without proteinuria. Angiotensin converting enzyme inhibitor or angiotensin receptor blocker is the preferred antihypertensive agents.

5. Use of angiotensin converting enzyme inhibitor

   Angiotensin-converting enzyme inhibitor has beneficial effects in patients with diabetic nephropathy and other renal diseases. These drugs slow progression independent of their effect on blood pressure. Angiotensin receptor blockers are a new class of drugs, which may be used in patients who are intolerant of angiotensin converting enzyme inhibitor. Studies on their effect are in progress.

   Angiotensin converting enzyme inhibitor reduces proteinuria, an effect that may—in itself—be renoprotective. These agents reduce proteinuria at any given level of blood pressure reduction more than other antihypertensive drugs. Risks associated with use of these drugs include dangerous hyperkalemia and acute renal failure when they are used in situations associated with decreased glomerular filtration pressure such as dehydration or renal artery stenosis. Careful monitoring of potassium levels and serum creatinine is warranted. (See Appendix 4 in the original guideline document)

6. Protein restriction

   Protein restriction appears to slow the progression of renal insufficiency and decrease symptoms and signs of renal insufficiency. Furthermore, some deferral of dialysis is achieved simply by reduction of symptoms and the severity of azotemia at any given level of renal function.

   The benefit of a low protein diet in slowing progression is controversial. Clinical trials suggest that dietary protein restriction may slow the progression of renal disease.

   A low protein diet (0.6 g/kg) without supplements may be less effective than a very low protein diet (0.3 g/kg) supplemented by essential amino acid (or ketoacid) tablets, 10 g/day in divided doses with meals, but raises additional problems of compliance and cost.

   Protein restriction also reduces proteinuria. In nephrotic patients, a progressive fall in proteinuria and rise in serum albumin may occur

over several months, especially if chronic kidney insufficiency (CKI) is not severe. This response was seen to a very low protein diet (0.3 g/kg) supplemented by essential amino acids (10-20 g/day in divided doses with meals), but not to a conventional low protein diet (0.6 g/kg).

7. Control of hyperglycemia in diabetics

   Refer to module G in the Veterans Administration/Department of Defense guideline: The Management of Diabetes Mellitus in the Primary Care Setting.

M. Prevent and Treat Symptoms and Complications (Metabolic Abnormalities, Hematologic Abnormalities, Volume Overload, and Nutrition)

Objective

To maintain normal metabolic levels and homeostasis in patients with renal disease.

Annotation

There are numerous complications and symptoms that may require treatment. The common metabolic and hematologic abnormalities are addressed here.

0. Metabolic Abnormalities

   Disorders of Potassium Balance

   Disorders of potassium (K) homeostasis (both high and low potassium levels) may result in preventable morbidity and mortality. Potassium levels should be checked periodically in patients with renal disease. (See Appendix 3 in the original guideline document)

   Hyperkalemia is a common disorder in patients with renal disease, especially when the glomerular filtration rate falls below 20 ml/min. Hyperkalemia may occur as a result of impaired tubular secretion of potassium (K) in patients with mild chronic kidney insufficiency. It is more prevalent among diabetics with type 4 Renal Tubular Acidosis and is frequently exacerbated by the use of certain drugs such as angiotensin converting enzyme inhibitors, angiotensin receptor blockers, NSAIDS, trimethoprim and non-selective beta blockers. Other contributing conditions include volume depletion leading to poor urine flow, severe hyperglycemia and starvation. Especially in diabetics, poor oral food intake (e.g. preoperative periods) resulting in low serum insulin levels may cause or exacerbate hyperkalemia. High intake of certain food items (see below) can also lead to hyperkalemia in patients with impaired renal function. Referral to a dietitian for a potassium-restricted diet is useful.

K > 6.5

Elevation of potassium (K) above 6.5 meq/L is a medical emergency and needs immediate attention to prevent life threatening cardiac arrhythmia.

K 5.5 - 6.5 mEq/L

A more conservative approach is generally acceptable if a rapidly reversible cause is identified (e.g. oral potassium supplementation) and the patient is symptomatic, without electrocardiogram (EKG) manifestations of hyperkalemia. Discontinuation of offending drugs, adequate nutrition, moderate potassium restriction and/or correction of prerenal azotemia or metabolic acidosis with sodium bicarbonate is frequently sufficient. Persistent hyperkalemia may require a more stringent dietary limitation although very low potassium diets (less than 40 meq/L/day) may lead to protein malnutrition. If the cause for hyperkalemia is not readily identifiable and the elevation in serum potassium is mild, other measures can be instituted in the outpatient setting. Liberalization of sodium intake, loop diuretics and thiazides may be used in selected patients although their side effects (volume depletion, hyperuricemia, etc.) must be taken into account. Another option includes the use of sodium polysterene sulfonate (SPS) or Kayexalate®. The usual dose for sodium polysterene sulfonate is 30 grams given with 100 mL of a 20% sorbitol solution. This can be repeated every 4 to 6 hours as needed. Lower doses (5 to 10 grams with meals) can be used to control chronic mild hyperkalemia. Fludrocortisone, a potent mineralocorticoid may be used in patients with type 4 renal tubular acidosis (RTA). Refractory hyperkalemia should prompt a referral to a nephrologist.

Potassium Content of Foods

- Highest content (>25 mEq/100 g) -- Dried figs, molasses, seaweed
- Very high content (>12.5 mEq/100 g) -- Dried fruit (dates, prunes) nuts, avocados, bran cereals, wheat germ, lima beans
- High content (>6.2 mEq/100 g)
    - Vegetables: spinach, tomatoes, broccoli, winter squash, beets, carrots, cauliflower, potatoes
    - Fruits: bananas, cantaloupes, kiwi, oranges, mango
    - Meat: ground beef, steak, pork, veal, lamb

Since the cause of hyperkalemia may be multifactorial and may differ from patient to patient, the choice of treatment of mild-to-moderate hyperkalemia may require different combinations of the recommendations.

After therapy is instituted, a follow-up potassium level should be performed within one week to ensure effectiveness of therapy and identify any need for further modification of the treatment regimen.

Hypokalemia K < 3.5

Hypokalemia may occur as a result of diuretic therapy or renal disease and may cause cardiac arrhythmia and muscle weakness. A fall in serum potassium of 1 mEq/L reflects a loss of about 200-400 mEq in total body potassium. Replacement by foods high in potassium (see above) is usually less effective than administration of oral potassium chloride (KCl). Slow release tablets or capsules can be used, in the following dosage: (a) for prevention of hypokalemia, potassium chloride 8-20 mEq/day; (b) for treatment of potassium depletion, potassium chloride 40-100 mEq/day.

Severe hypokalemia, defined as serum potassium level below 3.0 mEq/L, may require intravenous potassium replacement, especially in patients on digoxin or if it is anticipated that potassium losses will continue (e.g. vomiting, diarrhea, etc.) In the patient with renal disease, replacement should be approached with caution. High potassium chloride doses must be used with more frequent measurements of the serum potassium. IV potassium chloride replacement should be given no faster than 10 mEq per hour. It is preferable to replace potassium as a chloride salt as opposed to potassium-citrate of potassium-bicarbonate; one exception to this may be renal tubular acidosis (the hypokalemic types) and chronic diarrheal states.

Disorders of Calcium Metabolism

The goal of therapy is to normalize serum calcium (Ca) to avoid development of renal osteodystrophy as well as neuromuscular and cardiovascular complications.

Calcium balance is altered in renal disease patients. Low serum calcium is a salient feature of renal disease and is a component of the syndrome of secondary hyperparathyroidism. Secondary hyperparathyroidism starts early in renal patients, when serum creatinine levels are between 1.5 to 2.0 mg/dL. Low calcium levels result primarily from deficiency of 1,25,dihydroxyvitamin D; however, not all patients with hypocalcemia should be started on vitamin D preparations. Normocalcemia can be obtained in many patients by using measures other than vitamin D administration (see below).

Ca < 8.0 mg/dL

Hypocalcemia is rare in patients with renal disease unless the glomerular filtration rate falls below 30 ml/min. Calcium may be low because of an associated hypoalbuminemia. A useful correction of calcium concentration for hypoalbuminemia is corrected calcium (Ca) = Measured Ca + (4- serum albumin) x 0.8. Hypocalcemia is frequently the result of associated hyperphosphatemia and decreased levels of 1,25,dihydroxyvitamin D_3 levels. Along with hyperphosphatemia, hypocalcemia contributes to secondary hyperparathyroidism and renal osteodystrophy. Treatment of

hypocalcemia should be modified in response to phosphate levels. In patients with a serum phosphate above 4.5 mg/dL, we recommend the use of calcium based phosphate binders. Calcium carbonate (1250 mg tablets containing 500 mg of elemental calcium) given as one to four tablets three times a day with meals is also effective. Calcium carbonate may also be administered as 420 mg tablets containing 168 mg of elemental calcium. Calcium acetate (667 mg tablets, two to four tablets a day with meals) is also effective, but is more expensive. This will frequently raise serum calcium (although not necessarily normalizing it) by lowering serum PO_4. In hypocalcemic patients with normal serum phosphate, calcium-carbonate or calcium-acetate can be given between meals. The major side effect of these preparations is hypercalcemia.

Refractory hypocalcemia, especially in normophosphatemic patients, may require the use of calcitriol (1,25,dihydroxyvitamin D_3). This form of therapy is better instituted in consultation with the nephrologist, given the possibility that the patient may be suffering from "adynamic bone disease", in which case vitamin D treatment may be counterproductive). Correction of hypocalcemia through nutritional means, such as the use of dairy products, frequently results in an elevation of serum phosphate that is obviously undesirable.

Ca > 11 mg/dL

Spontaneous hypercalcemia is infrequent in chronic renal failure patients, most often resulting from underlying conditions such as myeloma, sarcoidosis and neoplasms. More commonly, hypercalcemia in this population is iatrogenic, resulting from the use of calcium-containing binders, either alone or in combination Vitamin D analogues. In patients treated with calcium carbonate or calcium acetate, temporary discontinuation or reduction of calcium-based binders usually results in normalization of serum calcium. It is important to remember that patients may be taking calcium carbonate (Tums®) to alleviate dyspepsia without recognizing them as a source of calcium. In patients not on exogenous calcium or vitamin D, the development of hypercalcemia should prompt the work-up for an underlying condition.

When the Ca x PO_4 product exceeds 70, there is a possibility of dangerous precipitation of Ca in non-osseous tissues. Use of Ca based PO_4 binders may transiently exacerbate the problem. Use of aluminum hydroxide (300 to 600 mg p.o. tid with meals) for periods not to exceed 7-10 days (to avoid Al^{3+} toxicity) may be necessary. When the Ca x PO_4 product falls below this dangerous level, calcium-carbonate or calcium-acetate may be started. RenaGel®, a new polymeric resin that does not contain calcium may be used, but its high cost and recent introduction will probably limit its use to the Nephrology Service.

<u>Disorders of Phosphate Metabolism (Hyperphosphatemia is serum phosphate (PO_4) >4.5 mg/dL)</u>

Adequate control of serum phosphorus is important for preventing the development of secondary hyperparathyroidism and the occurrence of soft tissue calcifications. Hyperphosphatemia has been identified as an independent risk factor for mortality in hemodialysis patients.

Hyperphosphatemia is at the center of the pathogenesis of secondary hyperparathyroidism and renal osteodystrophy. As renal disease progresses, retention of PO_4 leads to stimulation of parathyroid hormone (PTH) secretion resulting in high levels of osteoclastic and osteoblastic cell activity (high bone turnover), with increased deposition of extracellular bone matrix resulting in fibrosis. Measurement of serum phosphate level and serum calcium level four times per year is recommended.

Healthy individuals ingest about 1 to 1.8 grams of phosphorus a day. Patients with renal disease may require restriction to 0.8 to 1.2 grams of phosphorus a day. Use calcium carbonate or calcium acetate with meals (see treatment of hypocalcemia) when dietary restriction does not accomplish the target serum phosphate level of less than 4.5 mg/L.

Aluminum hydroxide should be used sparingly and for short duration to avoid aluminum loading and toxicity. Citrate based compounds should not be administered concurrently with aluminum based binders because they increase aluminum absorption in the gut, and may cause aluminum intoxication.

Hypoalbuminemia (Serum Albumin Less Than 3.5 g/dL)

Malnutrition in patients with renal failure is common. Mortality in dialysis patients correlates inversely with albumin levels. Early referral to a nutritionist is indicated in all patients with compromised renal function. Preferably patients should see a nutritionist at least twice a year and more frequently when they reach pre-end stage renal disease levels of glomerular filtration rate (< 20 ml/min). Protein intake may be assessed by 24-hour urinary urea nitrogen excretion (UN g/day).

Estimated Protein Intake (g) = [UN + (.031 x weight (Kg))] x 6.25

See the Annotation on Nutrition, below, for further information on the management of hypoalbuminemia.

Note: Rule out other coexisting disease e.g. liver disease, chronic infection, protein-losing enteropathy or occult malignancy.

Metabolic Acidosis (CO_2 <20 mEq/L and serum pH <7.40)

Metabolic acidosis is common in renal insufficiency and results from the accumulation of organic acids in plasma as well as impairment of renal acidification mechanisms. It is important to maintain serum HCO_3 (measured as plasma CO_2) above 20 mEq/L. Correction of metabolic

acidosis lessens renal osteodystrophy and improves protein metabolism.

Oral bicarbonate replacement in the form of $NaHCO_3$ tablets is indicated when the serum carbon dioxide falls below 20 mEq/L. The recommended dose of bicarbonate is 0.5 mEq/Kg/day, in divided doses. We recommend using 650 mg tablets (containing 7.7 mEq Na/7.7 mEq HCO_3^-). The target is to titrate serum carbon dioxide to 20 mEq/L. Na citrate is not recommended because it facilitates aluminum absorption through the gut, resulting in possible severe and acute aluminum toxicity.

1. Anemia

Anemia is a common consequence of chronic renal failure, usually caused by erythropoietin deficiency. Treatment of anemia improves exercise tolerance, decreases cardiovascular mortality, and promotes a sense of well-being. The evaluation of the cause of the anemia in patients with renal failure should be similar to that in patients without renal failure. Iron deficiency and gastrointestinal (GI) blood loss may be more common in patients with renal failure. Measurement of erythropoietin level is not indicated for suspected anemia of renal disease.

The usual diagnostic indices for iron deficiency may not be applicable in chronic renal failure. Chronic renal failure may result in an increase in serum ferritin due to the release of inflammatory cytokines. Although the exact value of serum ferritin that would exclude a response to iron therapy is controversial, there is evidence that treatment with iron in patients with serum ferritin up to 200 mg/ml may result in an increase in the hemoglobin-hematocrit ratio (Hb/Hct) in up to 50% of patients.

Therefore, we recommend determining serum ferritin in all renal failure patients with anemia, and treating with oral iron if the serum ferritin is <200 mg/ml. Although some investigators suggest using transferrin saturation (transferrin saturation % = serum iron x 100% / total iron binding capacity), most studies indicate that serum ferritin has better sensitivity and specificity for diagnosis. Oral iron should be given in a daily dose equivalent to 200 mg elemental iron (typically ferrous sulfate 325 mg tid) for six months.

If the cause of the anemia is identified and treated and the hemoglobin remains <10 gm/dl (or Hematocrit <30%), the patients should be referred to Nephrology/Hematology for further evaluation and consideration for epoietin therapy. Evidence suggests that treatment of renal failure patients to increase their hemoglobin to >10 gm/dL may improve quality of life and reduce cardiovascular morbidity. A patient who has a hemoglobin of 10-12 gm/dL, and no symptoms, should be followed with a repeat hemoglobin on a semi-annual basis or as clinical condition requires.

2. Volume Overload

   Volume overload should be suspected in patients complaining of dyspnea, chest discomfort, orthopnea, paroxysmal nocturnal dyspnea, or progressive decrease in exercise tolerance. It may also be asymptomatic. Physical findings could include jugular venous distention, hepatojugular reflux, pulmonary rales, wheezing (in "cardiac asthma"), and S3 or S4, ascites, and peripheral edema. Patients with chronic renal failure may also have significant volume overload even in the absence of the above symptoms and signs. Chest films may show evidence of pulmonary edema or may be subtle, showing only prominent pulmonary vasculature. The same findings may occur with heart failure, liver failure and various other conditions, so the patient's change in weight over time is critical. Over weeks to months, these patients may lose lean body mass due to malnutrition and can develop fluid overload with relatively little change in weight. Therefore, serial assessment of patients' lean body mass is also critical.

   Contributors include:

   - Excess salt intake
   - Progressive renal damage (nephrosclerosis)
   - Fluid retention from blood pressure medications
   - Inadequate diuretic therapy.

   Consider fluid overload for sudden unexplained gains in weight, refractory hypertension, peripheral edema or shortness of breath. These may be secondary to the above causes. Hyponatremia, developing as a result of water retention in excess of sodium retention, may also be a marker for volume overload in the above setting

   Management:

   - Patients should be weighed at every visit
   - Dietary sodium restriction to 2 gm/d
   - Loop diuretics, and if refractory to twice a day dosing, consider adding thiazide-type diuretics
   - If advanced renal failure, consider initiation of dialysis

Annotation

All patients with chronic renal disease should have an assessment by a renal dietitian soon after diagnosis. Attention should be given to overall nutrition, including lipids, potassium, phosphate, sodium, protein and energy. In patients with early or moderate renal insufficiency, daily energy intake should be 35 kcal/kg body weight and daily protein intake should be 0.8 g/kg body weight. For patients with more severe renal insufficiency or nephrotic syndrome, severe protein restriction in conjunction with a dietary supplement may be useful to prevent symptoms and reduce proteinuria.

N. Prevent and Treat Cardiovascular Disease

Objective

To improve cardiovascular health in patients with renal disease, enhance their quality of life and improve survival rates for patients that progress on to end stage renal disease and dialysis and/or transplantation.

Annotation

Patients with renal disease and/or proteinuria are at high risk for cardiovascular disease. Modification of risk factors may attenuate these risks. Effective treatment of hypertension, hyperlipidemia and anemia, along with smoking cessation and exercise, are essential.

For the treatment of hypertension, please review the Veterans Administration/Department of Defense Guideline for the Management of Hypertension in Primary Care.

For control of dyslipidemia, please refer to the Veterans Administration/Department of Defense Guideline for the Management of Dyslipidemia in Primary Care.

For the treatment of anemia see Annotation M.

For the treatment of smoking cessation, please refer to Veterans Administration/Department of Defense guideline on Tobacco Use Cessation.

For additional information on prevention and treatment of cardiovascular disease, refer to the Veterans Administration/Department of Defense Guideline for the Management of Ischemic Heart Disease.

Veterans Administration/Department of Defense guidelines can be found on the Veterans Administration Web site.

O. Provide Patient Education

Objective

To enhance patient adherence to treatment.

Annotation

Patient education should begin soon after the diagnosis of renal insufficiency. The importance of strategies to delay progression of renal disease and avoid further renal injury must be highlighted.

Few renal disease education curricula have been published. The Canadian Pre-Dialysis Advisory Board developed one such program. Oschner Clinic Renal Services developed a pre-end stage renal disease education program in 1997

called "Healthy Start" that may serve as a resource. Both programs have received support from Baxter Healthcare Renal Division through their Pre-End Stage Renal Disease Education Program. This program provides a nurse educator, at no charge, to interested hospitals, clinics, or physicians.

Key areas that need to be included in the education program for patients and their families are discussed below. Items 1-7 should be covered early in the course of renal insufficiency. The others may be covered later, as renal insufficiency progresses and additional complications become likely.

0. General overview

   Anatomy and normal function of the kidneys, altered renal function and the patient's disease process need to be explored. Laboratory tests and results, diet and medications should be reviewed. This can be done in small groups. Groups may be inappropriate, however, for patients who have low literacy skills or learning problems.

1. Control of blood pressure

   Adherence to medications and dietary and lifestyle changes may reduce the rate of progression of renal disease as well as reduce the risk of cardiac disease. For further information on this topic, please see the Veterans Administration/Department of Defense Clinical Guideline for the Management of Hypertension, Annotation K.

2. Low protein diet

   There are several clinical trials that have suggested delay in the progression to end stage with moderate protein restriction to 0.6 gm/kg/day, although conclusive evidence is lacking. See section on nutrition, Annotation M.

3. Blood glucose control

   Among diabetics, large-scale trials suggest delay in progression as well as amelioration of other complications of diabetes. See the Veterans Administration Clinical Guideline for Management of Diabetes Mellitus, Module G.

4. Angiotensin converting enzyme inhibitors

   There is mounting evidence that use of angiotensin converting enzyme inhibitors delays progression of diabetic and non-diabetic renal disease, even in the absence of hypertension. There are the potential risks of developing hyperkalemia and worsening renal function (especially if there is renal vascular stenosis). Thus, initiation of this treatment must be done with close follow-up to monitor potassium and creatinine, and continuation may require dietary potassium restriction. Patients on angiotensin converting enzyme inhibitors must be advised of the increased risk of acute renal failure in the setting of volume

depletion, such as may be seen with protracted vomiting, diarrhea or high fevers. In such instances, patients must be instructed to seek evaluation.

5. Avoidance of NSAIDS and other nephrotoxic drugs, including illicit drugs

   Patients should be counseled about the possible adverse consequences of nonsteroidal anti-inflammatory drugs, which are in many over-the-counter cold and pain preparations. They need to understand that the kidney is a frequent target for toxic injury because it is a major route of excretion for a variety of drugs. It is also important to obtain a history of any alternative medical therapies the patient may be using. It has been reported that only 30% of patients who use alternative therapies ever mention it to their health care providers. Therefore it is important to attempt to establish rapport, so that the patient will share information. Occupational and environmental exposures as well as the use of cocaine, heroin, and amphetamines (Ecstasy) need to be explored as well.

6. Lifestyle changes

   Patients may need to make lifestyle changes in such areas as: smoking cessation, weight control, other dietary changes, drug and alcohol treatment, increased physical activity, stress management, social issues, vocational rehabilitation, family issues and issues of sexuality.

   These changes may take a concerted team effort and may require on-going support groups. Repetitive contact, monitoring, and encouragement are all methods to reinforce behavior change. See the Clinical Guideline for the Management of Diabetes Mellitus, Module R, Renal Disease. Also see Module H for suggestions on smoking cessation, exercise, and stress management.

7. Abnormal calcium and phosphate metabolism

   These may lead to bone disease, resulting in pain and fractures, and the deposition of Ca and PO_4 in microvasculature, leading to tissue ischemia and loss. Patients should be advised about the importance of the control of calcium and phosphate for the prevention of bone and cardiovascular disease.

8. Anemia secondary to relative erythropoietin deficiency

   Anemia is associated with the development of left ventricular hypertrophy and congestive heart failure (CHF), both of which may increase cardiovascular mortality among patients with renal failure, but which may be ameliorated by improvement in the anemia with iron or erythropoietin (EPO). Treatment of anemia may also maintain normal cognitive function.

9. Hyperkalemia related to reduced clearance

   Hyperkalemia usually does not develop until late in the course of renal insufficiency, once the glomerular filtration rate falls below 20 ml/min or oliguria has developed. However, earlier development of hyperkalemia may occur among patients with diabetic nephropathy (or other conditions associated with hyporeninemic hypoaldosteronism, such as chronic interstitial nephritis), and patients on angiotensin converting enzyme/angiotensin receptor blockers (ACE-I/ARBs), NSAIDS or potassium-sparing diuretics. Formal dietary counseling is recommended for potassium restriction for hyperkalemia that does not resolve with discontinuation of possible culprit medications. Potassium-binding resins may be necessary, along with close monitoring as renal failure progresses. Patients must be told that significant hyperkalemia predisposes to cardiac dysrhythmias and death.

10. Preparation for Kidney Replacement Therapy

    Once there is evidence of progression of kidney insufficiency, or at the latest when the creatinine is $\geq$ 3 mg/dL or the creatinine clearance is $\leq$ 40-50 ml/min, the patient must be instructed to 'save' the non-dominant arm for hemodialysis access (no venipuncture or IV), and physicians must avoid central lines (in particular subclavian, but also internal jugular (IJ) given the risk of IJ or superior vena cava (SVC) stenosis).

    The various modalities of kidney replacement therapy, including hemodialysis, peritoneal dialysis and preemptive transplantation, should be introduced once there is clear evidence of progression to kidney replacement therapy. There are currently no age restrictions on the initiation of dialysis, thus the decision to withhold dialysis must be made in conjunction with a well-informed patient. The patient should also be referred to nephrology for full discussion of these issues—at the latest when the creatinine is $\geq$4 mg/dl or the creatinine clearance is $\leq$30 ml/min—to enable realistic exploration of living donor transplant prior to the requirement for dialysis.

P. Follow-up

Objective

To detect early changes in kidney function, clinical status, and biochemical parameters in order to prevent or to attenuate uremic complications and, possibly, to slow the progression of renal disease.

Annotation

The frequency of follow-up visits depends on the severity of renal disease. It is unlikely that patients with mild renal insufficiency (serum creatinine<2.0 mg/dL) will develop electrolyte disturbances, anemia or uremic bone disease. Similarly, patients with normal renal function and mild proteinuria (<1.0 g/24

h), in the absence of diabetes mellitus, are less likely to develop more serious renal problems. These patients, if they do not have other co-morbidities and if their renal function has been stable, can be seen about two to three times per year.

It is advisable that a nephrologist be consulted, at least initially, for the care of patients with more advanced renal insufficiency (serum creatinine > 2.0 mg/dL or glomerular filtration rate < 50 ml/min) and for patients with larger amount of proteinuria. Patients with nephrotic range proteinuria (>3g/24h) need additional work-up that may include renal biopsy. There is a high possibility that renal insufficiency will progress to end-stage-renal-disease in patients with serum creatinine greater than 2 mg/dL (or glomerular filtration rate less than 50 ml/min). Many biochemical abnormalities that will eventually lead to clinical symptoms associated with uremia are already detectable at this level of glomerular filtration rate. Education about end stage renal disease and treatment options should be given to these patients. Dietary protein restriction may be helpful in preventing uremic symptoms and in delaying the progression of renal disease in patients with chronic renal failure. Low protein diet can also reduce proteinuria in patients with nephrotic syndrome. In addition to dietary protein restriction, attention should be given to overall nutritional status, hyperlipidemia and electrolyte balance. These patients should be seen by a renal nutritionist at least twice yearly. They also need more frequent follow-up (usually every 2 to 3 months) in the clinic. The care of these patients could be transferred to a specialty clinic or could be coordinated between primary care physicians and the specialty clinic.

Patients with serum creatinine greater than 4 mg/dL (glomerular filtration rate <25 ml/min) have severe renal insufficiency and should be referred to a nephrologist without any delay. These patients are at high risk of developing uremic complications. They could also progress to end stage renal disease in a relatively short time. By this time the patient should have a good knowledge about end stage renal disease and its treatments. If hemodialysis is the treatment option, the patient should receive the instruction not to use the non-dominant arm for blood drawing. An exercise program to build up forearm muscle and to increase the size of forearm veins should be instituted. A permanent vascular access (preferably an arteriovenous [AV] fistula) should be placed when the glomerular filtration rate is ~ 15 ml/min (20 ml/min in diabetics). If preemptive kidney allograft transplantation is an option, work-up for the patient and potential donors must be initiated. These patients obviously need frequent follow-up, usually every one to two months. They also need to be evaluated more frequently by a nutritionist.

Frequent follow-up visits are also indicated in patients with rapid change in renal function or in whom there are not enough data to determine the rate of progression of renal failure. Other groups of renal patients who need to be seen frequently are patients with poorly controlled blood pressure and diabetic patients with poorly controlled blood pressure or blood sugar, or both. Poorly controlled blood pressure (BP) (blood pressure >130/80 mmHg) can adversely affect the progression of renal disease in diabetics as well as in patients with renal insufficiency from other causes. Poor glycemic control may also adversely affect the progression of diabetic renal disease. It may be necessary to see these patients and to adjust their medications at least

monthly until their blood pressure readings and/or their blood sugar are in the acceptable ranges. If hypertension or diabetes mellitus is difficult to manage, a consultation with a specialist may be appropriate. See the Veterans Administration/Department of Department guidelines for hypertension and diabetes mellitus for more details.

Serum electrolytes, blood urea nitrogen/creatinine, calcium/phosphorous (Ca/P), serum albumin and urinalysis should be done routinely at each visit. An asymptomatic patient with a stable level of hemoglobin (Hgb) at 10 g/dL or more should have his/her hemoglobin checked at least twice yearly. In diabetic patients who do not have macroalbuminuria, determination of microalbuminuria should be done at least yearly.

CLINICAL ALGORITHM(S)

A clinical algorithm is provided for Management of Chronic Kidney Disease and Pre-End Stage Renal Disease (ESRD) in the Primary Care Setting.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The guideline is supported by the literature in a majority of areas, with evidence-based tables and references throughout the document. The evidence consists of key clinical randomized controlled trials and longitudinal studies in the area of chronic renal disease. Where existing literature is ambiguous or conflicting, or where scientific data are lacking on an issue, recommendations are based on the expert panel's opinion and clinical experience. The guideline contains a bibliography and discussion of the evidence supporting each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved identification of patients at risk for progression of renal disease or patients with reversible conditions
- Lowered rate of progression of renal disease
- Fewer complications of renal disease and improved treatment of complications when they occur
- Improved rate of referral to specialty care
- Improved patient acceptance and compliance with treatment

POTENTIAL HARMS

Side effects of pharmacotherapy. In particular, there are the potential risks of developing hyperkalemia and worsening renal function with the use of angiotensin-converting enzyme inhibitors (ACEIs), especially in patients with renal vascular stenosis. Side effects and cautions of other medications commonly used in patients with renal disease are tabulated in Appendix 4 of the original guideline.

Subgroups Most Likely to be Harmed:

Patients with renal vascular stenosis are at increased risk of developing hyperkalemia and worsening renal function with the use of angiotensin-converting enzyme inhibitors.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Clinical practice guidelines, which are increasingly being used in health care, are seen by many as a potential solution to inefficiency and inappropriate variations in care. Guidelines should be evidenced-based as well as based upon explicit criteria to ensure consensus regarding their internal validity. However, it must be remembered that the use of guidelines must always be in the context of a health care provider's clinical judgment in the care of a particular patient. For that reason, the guidelines may be viewed as an educational tool analogous to textbooks and journals, but in a more user-friendly format.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Veterans Health Administration, Department of Defense. VHA/DoD clinical practice guideline for the management of chronic kidney disease and pre-ESRD in the primary care setting. Washington (DC): Department of Veterans Affairs (U.S.), Veterans Health Administration; 2001 May. Various p.

ADAPTATION

The guideline draws, in part, from the NKF-DOQI clinical practice guidelines (the National Kidney Foundation-Dialysis Outcomes Quality Initiative, 1997).

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2000 November

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Management of Renal Failure Working Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

ENDORSER(S)

Veterans Health Administration National Clinical Practice Guideline Council - Federal Government Agency [U.S.]

GUIDELINE STATUS

This is a current release of the guideline.

An update is targeted for late 2003.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Veterans Health Administration (VHA) Web site.

Print copies: Available from the Department of Veterans Affairs, Veterans Health Administration (VHA), Office of Quality and Performance (10Q), 810 Vermont Ave. NW, Washington, DC 20420.

AVAILABILITY OF COMPANION DOCUMENTS

Various companion documents are available from the Veterans Health Administration (VHA) Web site.

In addition, the VHA Web site provides references to related guidelines, performance measures, and other resources.

Also available:

- Guideline for Guidelines. Draft. Washington (DC): Veterans Health Administration, Department of Veterans Affairs. Available at: VHA Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 9, 2002. The information was verified by the guideline developer on September 25, 2002.

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